

REPLY TO FINAL OFFICE ACTION

Atty. Dkt. No. 061537-0036

U.S. Serial No.: 10/724,292

Filing Date: 1 December 2003

Title: Recombinant Adenoviral Vectors And Their Utility  
In The Treatment Of Various Types Of Fibrosis: Hepatic,  
Renal, Pulmonary, As Well As Hypertrophic Scars

**AMENDMENTS TO THE CLAIMS**

**This listing of claims will replace all prior versions and listings of claims in the application:**

1.-21. (Canceled)

22. (Currently amended): A pharmaceutical composition to treat hepatic fibrosis in a human comprising a therapeutically effective amount of unitary doses of viral particles of recombinant adenoviral vectors,

wherein said unitary dose is from about  $10^7$  to about  $10^{14}$  viral particles;

wherein the adenoviral vectors comprise an adenoviral genome of serotype Ad5 with deletions at E1 and inserted with a DNA sequence regulated by a ubiquitous promoter, a tissue-specific promoter, or a combination thereof, and wherein the DNA sequence encodes for a therapeutic protein for the treatment of hepatic fibrotic disorders;

and a pharmaceutically compatible carrier;

wherein the composition is suitable for intravenous administration; and,

wherein the therapeutic protein for the treatment of fibrotic disorders is selected from the group consisting of human matrix metalloprotease-8 (“MMP-8”), human matrix metalloprotease-1, human matrix metalloprotease-2, human matrix metalloprotease-9, matrix metalloprotease-13 and combinations thereof and the truncated receptor for human transforming growth factor- $\beta$  (“TGF- $\beta$ ”) type II.

23. (Canceled).

24. (Currently amended): A method of treating fibrotic disorders in a human patient, comprising:

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delivering the composition of claim 22 by an intravenous administrative route to ~~an organ~~  
a liver; and

expressing the therapeutic protein in the liver from the recombinant adenoviral vector of  
the composition to treat the hepatic fibrotic disorders.

25.-27. (Canceled).

28. (Previously presented): The pharmaceutical composition according to claim 22,-wherein  
the therapeutic protein for the treatment of fibrotic disorders is MMP-8.
29. (Previously presented): The pharmaceutical composition according to claim 22, wherein  
the therapeutic protein for the treatment of fibrotic disorders is MMP-1.
30. (Previously presented): The pharmaceutical composition according to claim 29, wherein  
the therapeutic protein for the treatment of fibrotic disorders is the truncated receptor for  
TGF- $\beta$  type II.
31. (canceled)
32. (Previously presented): The pharmaceutical composition according to claim 22, wherein  
the therapeutic protein for the treatment of fibrotic disorders is matrix metalloprotease-2.
33. (Previously presented): The pharmaceutical composition according to claim 22, wherein  
the therapeutic protein for the treatment of fibrotic disorders is matrix metalloprotease-9.
34. (Previously presented): The pharmaceutical composition according to claim 22, wherein  
the therapeutic protein for the treatment of fibrotic disorders is matrix metalloprotease-13.